By the present amendments, claim 44 has been amended to expedite prosecution.

Turning now to the Office Action, claims 44-46 and 49-55 stand rejected under 35 U.S.C. §1.112, first paragraph, based on lack of written description. It is anticipated that this rejection will be withdrawn upon entry of the present amendment to claim 44. Particularly, clause (ii) of claim 44 has been amended such that it substantially finds verbatim written description support from the deformation of "prolonged suppression" at page 12, last paragraph of the specification which reads as follows:

"As used herein, "prolonged suppression" means that suppression of antibody production against a TD antigen is maintained after administration of a gp39 antagonist in vivo has been terminated".

Therefore, as the amendatory language finds verbatim support from the as-filed specification, withdrawal of the written description rejection is earnestly solicited.

Claims 44-46, 49 and 51-58 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Cobbold et al. in view of Lederman et al. or Armitage et al. The rejection is maintained for the reasons of record.

Claims 50, 54 and 55 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Cobbold et al. in view of Lederman et al., or Armitage et al., in view of Ramanathan et al.. This rejection is also repeated for the reasons of record.

Essentially, the Examiner's position remains that Lederman and Armitage respectively teach the use of gp39 antagonists to suppress humoral immunity and that in view of Cobbold it would have been reasonably expected that T cell tolerance and prolonged humoral suppression would result because of similar effects being achieved by the administration of antibodies to CD4. This rejection is respectfully traversed.

Contrary to the Examiner's assertions, there was no "reasonable expectation of success" to achieve the claimed limitations, i.e., prolonged humoral suppression.

As previously argued, Lederman and Armitage only suggest that humoral immunity to antigens could be suppressed in a transient manner, i.e., by administering a gp39 antagonist to a subject in need of such treatment. The fact that a gp39 antagonist, like CD4 antibodies binds an antigen or activated helper T cells, is insufficient to suggest that humoral immunity would remain suppressed after administration of the gp39 antagonist has been terminated.

This could not have been predicted as neither Armitage or Lederman remotely alludes to the fact that a gp39 antagonist would induce tolerance or prolonged suppression of

humoral immunity.

With respect thereto, the Examiner alleges that this would have been expected given the essential role of helper cells immune responses and immune regulation. However, this position is also respectfully traversed.

The prior art only suggest that CD4 antibodies can be used to induce T cell tolerance. This is not sufficient to establish with a reasonable likelihood of success that antibodies to another T helper cell antigen, or gp39 in particular would induce prolonged suppression of immunity, i.e., tolerance.

In fact, the rejection ignores the unpredictability with respect to achieving tolerance that existed at the time of the invention. As evidence of this fact, Applicants attach hereto two abstracts, Schonrich et al., Int. Immunol 4(5)581-90 (1992) and Schneider et al., Thymus 20(1):5-15 (1992) which disclose that the induction of tolerance as of 1992 was unpredictable, and varied dependent upon the particular (tolerizing) antigen. Hence, the fact that CD4 induced tolerance, would not be sufficient to suggest that an anti-CD40L would induce tolerance, especially as the induction of tolerance and the mechanisms associated therewith were poorly understood at the time of the invention. Therefore, Applicants respectfully submit that the prior art rejections based on the Armitage, Lederman and Cobbold patents should be vacated.

Respectfully submitted,

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Attachment: Appendix

APPENDIX

IN THE CLAIMS:

44. (Three Times Amended) A method for inducing prolonged humoral suppression in a subject in need of such prolonged humoral immune ~~response~~ suppression, to a soluble thymus dependent (TD) antigen which method comprises:

(i) administering a soluble TD antigen to which a humoral response is to be suppressed; and

(ii) administering an amount of an anti-gp39 antibody or a fragment thereof that binds gp39, in an amount effective to provide for prolonged humoral immune suppression to said soluble TD antigen, wherein administration of (i) and (ii) is effected concurrently , and wherein prolonged humoral immune suppression means that suppression of antibody ~~prevention~~ production against ~~the~~ said TD antigen is maintained after administration of a gp39 antagonist, wherein said gp39 antagonist is an ~~said~~ anti-gp39 antibody in vivo, has been terminated.